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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,687	05/11/2006	Jian Ding	035394-0306	2990

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,687	DING ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/6/05;1/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-56 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant desires a method for the detection of galectin-3 as a biomarker in patients with myocardial infarction. In this regard, applicant presents patterns obtained from serum samples from 4 known myocardial infarction patients (see e.g. Figs. 1A and 1B). Applicant does not describe and does not support the general applicability of the findings for one to practice the method for diagnosis of myocardial infarction with any predictability of success. For example, no indication is given as to the proportion of patients with severe myocardial infarction that

demonstrated presence of the marker, even in serum samples, in comparison with the proportions of control patients or patients with mild myocardial infarction or patients with other conditions that demonstrated presence of the biomarker in serum. No description or indications are given with regard to any differences in the levels of galectin-3 in samples from the different patient populations. No description or guidance is given for the selection of a sample other than serum. No description or guidance is given for the presence or level of the marker before a cardiac event relative to its level or presence after the event in any given patient. Thus, no description or guidance is given for the selection of a particular patient population for which the test has any relevance other than with a serum sample from a patient apparently known to have had a severe myocardial infarction. In this regard, mere detection of galectin-3 in a patient sample would not indicate a myocardial infarction in that patient because the marker is known to be present in older individuals (Prolla et al. (US 7,041,449)) or in patients with inflammation (Rabinovich et al. (Biochimica et Biophys. Acta 1572: 274, 2002)) or in patients with various diseases such as cancer (see e.g.: Woo (US 2002/0076738); or, Hsu et al. (US 2002/0155513)) or cirrhotic liver (Hsu et al. (US 2002/0155513)) or rheumatoid arthritis (Ohshima et al. (Arthritis Rheum. 48: 2788, 2003)). Absent further written description and guidance from applicant one would not know how, when, or with what patients or samples to perform the method as suggested and one would have no assurance of the ability to practice the method for diagnosis of myocardial infarction with any predictability of success.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is

granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Claims 37, 38, 41, 42, 50, and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claims appear drawn to a single antibody reagent that can bind galectin-3, fibrinogen, and/or tropinin-I. Applicant's specification does not provide written description for such reagents and does not teach how to make such reagents. Absent further written description and guidance from applicant one would have no assurance of the predictable ability to make and use antibody reagents as are instantly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23, 27-45, 48-51, and 54-56 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, the relationship of the correlating step to qualifying status, as set forth in the preamble, is not clear.

In claim 2 it is not clear how treatment is based on status.

In claim 3, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 5, "the" presence, absence, degree, or effectiveness lack antecedent basis.

In claims 8-10, the relationship of measuring to "detected" is not clear.

In claim 11, "the" presence, absence, amount, or type lack antecedent basis. Moreover, the relationship of a "type" of biomarker to the galectin-3 recited in claim 1 is not clear.

In claim 12, "using" is not a proper method step, --with-- is suggested.

In claim 18, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 19 and claims dependent thereupon, "the subject" lacks antecedent basis.

In claim 22, the relationship of measuring to "detected" is not clear.

In claim 23, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 27, the relationship of measuring to "detected" is not clear.

In claim 28, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 29 and claims dependent thereupon, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

In claim 36, it is not clear which of the previously recited capture reagents is "the" reagent intended.

In claim 38, the relationship of an anti-troponin-I antibody to a capture reagent that binds galectin-3 or fibrinogen is not clear.

In claim 41, the relationship of an anti-troponin-I antibody to a capture reagent that binds fibrinogen is not clear.

In claim 42, the relationship of an anti- galectin-3 antibody to a capture reagent that binds fibrinogen is not clear.

In claim 48, it is believed --one-- was intended.

In claims 49-51, the relationship of an antibody to a capture reagent that binds galectin-3 and fibrinogen is not clear.

In claims 54-56, the instructions further limit the intended use of the kit components and provide no further limitation of the kit components themselves.

In claim 54, "the" diagnosis lacks antecedent basis.

In claims 55 and 56, "the" result lacks antecedent basis.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claims 1-5, 7, 11, 12, 16-19, 22-24, 27-31, and 45 are rejected under 35 U.S.C. § 102(e)(2) as being clearly anticipated by Prolla et al. (US 7,041,449).

Prolla et al. teach detection or measurement of biomarkers in biological samples such as tissue samples, including heart, or in bodily fluids such as serum or plasma (see e.g. col. 4 and 7) to monitor treatments (see e.g. col. 7) or disease states (see col. 9). Nucleic acids encoding the biomarkers or biomarker proteins are detected. For detection of proteins, antibodies specific for the protein can be used in any suitable assay such as an ELISA, an immunohistochemical assay, or a proteomic assay such as mass spectroscopy (see e.g. col. 4 and 7). Analysis and presentation of results can be automated for example with software (see col. 4). Kits for identification, characterization, and quantitation of the markers are provided, including kits containing antibodies specific for the markers, other reagents such as buffers and detection reagents, controls, and instructions (see e.g. col. 7). A preferred biomarker for detection or measurement is galectin-3 (X16834) (see e.g. col. 8 and 14).

Claims 1-5, 7, 11, 16, 19, 22, 24, 27, 29-31, and 45 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Nachtigal et al. (Am. J. Pathol. 152: 1199, 1998).

Nachtigal et al. provided samples from normal patients and patients with atherosclerosis and detected galectin-3 by immunohistochemical staining or Western blotting with a monoclonal antibody specific for galectin-3.

Claims 19, 22-24, 27-31, and 45 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Liu et al. (Am. J. Pathol. 147: 1016, 1995).

Liu et al. teach immunoblotting, immunohistochemistry, and enzyme-linked immunosorbent assays for detection of galectin-3 in samples. Recombinant galectin-3 was provided as a standard.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-5, 7-19, 22-24, 27-37, 43-47, and 52-55 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Prolla et al. (US 7,041,449) in view of Issaq et al. (Biochem. Biophys. Res. Comm. 292: 587, 2002) and Liu et al. (Am. J. Pathol. 147: 1016, 1995).

The teachings of Prolla et al. are as set forth above and differ from the invention as instantly disclosed and/or claimed in not specifically teaching surface enhanced laser desorption/ ionization (SELDI) for use with the mass spectroscopy for the proteomic assay for protein detection or measurement.

Issaq et al. teach the SELDI-TOF mass spectrometry approach to proteomics and teach protein chips for capture of proteins for detection of biomarkers.

The teachings of Liu et al. are as set forth above. It is noted that the ELISA assay was performed in wells of a microtiter plate.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used the chips and methods taught in Issaq et al. with a reasonable expectation of success for the detection of the biomarkers in the kits and methods of Prolla et al. in view of the direct suggestions in the references to use proteomic assays involving mass spectrometry for the detection of biomarkers. One of ordinary skill in the art would have expected multiple different proteins to be immobilized by the protein chips taught in Issaq et al. in the kits and methods of Prolla et al., as modified. Alternatively, for the immunoassays of Prolla et al. it would have been obvious to have used a notoriously old and well known solid support such as a microtiter plate for an assay such as an enzyme-linked immunosorbent assay as taught in Liu et al. with well known antibody reagents specific for galectin-3 as taught in Liu et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 1-7, 11, 16, 19-22, 24-27, 29-31, 33, 34, 36, 37, 39, 40, 42, and 45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Nachtigal et al. (Am. J. Pathol. 152: 1199, 1998) and Bini et al. (Arteriosclerosis 9: 109, 1989).

The teachings of Nachtigal et al. are as set forth above and differ from the invention as instantly claimed in not teaching the dual detection of galectin-3 and fibrinogen.

Bini et al. teach the immunohistochemical detection of fibrinogen and fragments thereof in samples from normal patients and patients with atherosclerosis with monoclonal antibodies specific for the antigens.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used the reagents of Nachtigal et al. and Bini et al. in a dual staining method for the detection of multiple antigens indicative of atherosclerosis. One of ordinary skill in the art would have been motivated to use the successful methods in combination in a method of diagnosis because determinations of these analytes had been taught individually or in different combinations by the prior art to be effective in the diagnosis of atherosclerosis and it would have been obvious to diagnose atherosclerosis with both markers because the idea of doing so would have followed logically from their having been individually taught in the prior art to be useful for the same purpose.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Woo (US 2002/0076738) teaches the detection of galectin-3 in the blood of cancer patients.

Hsu et al. (US 2002/0155513) teach the detection of galectin-3 in cancer patients.

Liu et al. (US 2002/0044932) teach galectin-3 in inflammatory cells and the role of inflammatory cells in inflammatory injury occurring after reperfusion of ischemic tissue such as the heart (see e.g. [0050]).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
June 12, 2008

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641